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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,254	06/25/2003	Chih-Ming Chen	300.1003CON	3690

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,254	CHEN ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Remarks filed 2/10/05, the Terminal Disclaimer filed 2/14/05, and the Information Disclosure Statement of 4/7/05 is acknowledged. Claims **76-87** are pending in this application.

Double Patenting

The provisional rejection of claims 76-87 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 18-19, 21-22, 25-29, 31-47, 76-77, and 80 of copending Application No. 09/435576 is withdrawn in view of the Terminal Disclaimer filed.

Claim Rejections - 35 USC § 103

The rejection of claims 76-87 under 35 U.S.C. 103(a) as being unpatentable over Alberts et al (4,997,658) is withdrawn in view of applicant's arguments that Alberts teaches reducing the amount of HMG-CoA reductase in the blood serum level.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 76-87 under 35 U.S.C. 103(a) as being unpatentable over US patent 5,837,379 to Chen et al is maintained.

Chen et al disclose a once daily pharmaceutical tablet having a 1) compressed core containing a medicament, a water-soluble osmotic compound, and one or more osmotic polymers, and 2) a membrane coating containing a water insoluble pharmaceutically acceptable polymer and an enteric polymer. See abstract. Chen teaches various water-insoluble medicaments that may be utilized, including instant lovastatin. See column 2, line 64. The composition may additionally have dispersants, lubricants, dyes, and other additives that are conventionally utilized in the art. See column 5, lines 63-65. More specifically, Chen et al teach that the medicament granules contain nifedipine, povidone (osmotic polymer), lactose (osmotic agent), and sodium lauryl sulfate (surfactant). The granules are compressed with lactose, Polyox WSR, and Myvaplex and coated with a color coating contains dye, sodium chloride, and water. The color coating is coated with a sustained release coating; followed by an enteric coating containing HPMC phthalate, pore forming agent, talc, and plasticizer. See examples. Lastly it should be noted that lovastatin hydrolyzes in vivo to form its acid form, lovastatin acid.

Chen does not exemplify lovastatin in the controlled release device nor specify the instant functional limitations.

It is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Chen et al and include the instant lovastatin in the controlled release dosage form. One would have been motivated to do so since Chen teaches a variety of medicaments that would benefit from the use of the instant controlled release formulation and

teaches the instant active as one of the suitable medicaments. Therefore, one could reasonably expect similar results by including lovastatin in Chen's controlled release device.

Furthermore, it is the examiner's position that the instant controlled release device would meet the instant functional limitations since Chen's controlled release device is similar in structure and formulation to applicant's dosage form described in the specification; in particular Table 1. Therefore, it is the examiner's position that both would function similarly if not the same since the structures of the instant invention and that of the prior art are the same.

Response to Arguments

Applicant argues that Chen's controlled release device and the instant invention differ in formulations since the instant invention has different percentages and ingredients. Further, applicant argues Chen does not exemplify the instant lovastatin and merely suggests it in an exhaustive list. Applicant argues that Chen does not teach increasing the bioavailability of lovastatin.

Applicant's arguments filed 2/10/05 have been fully considered but they are not persuasive. Firstly, the examiner points out that applicant is broadly claiming a controlled release device without any distinguishing features except that the controlled release device provides a higher bioavailability, therefore the examiner refers to the specification to provide for a general formula, i.e. Table I. The examiner points out that Chen teaches a core containing the drug, povidone (a water-swellable polymer), an osmotic agent (lactose), and sodium lauryl sulfate (surfactant) in applicant's amount disclosed in Table I. The core is coated with a color coating containing a dye and sodium chloride (osmotic agent). The prior art's color coat is comparable to applicant's seal coat. Then a sustained release coating containing Eudragit S (enteric polymer),

and a plasticizer in applicant amount disclosed in Table I. The prior art's sustained release coat is comparable to applicant's inner coat. Lastly, the tablet is again coated with an enteric coating polymer containing an enteric polymer, a pore-forming agent (channeling agent), acetyltributyl citrate (plasticizer). The prior art's enteric coat is comparable to applicant's overcoat. Therefore, it can be seen that this device is the same as the described in instant specification of the preferred controlled release device that provides functional limitations of the instant application. Thus, it is the examiner's position that Chen's controlled release device would function similarly. It is pointed out that the examiner has provided a rationale that the prior art would function the same; thus the burden has shifted to applicant to prove otherwise. As noted in *In re Best*, the Patent Office can require the applicant to prove that a subject matter shown in the prior art does not possess a characteristic when there is reason to believe that the functional limitation asserted to be critical in establishing novelty in the claimed subject matter, is possessed by the prior art. The examiner suggests the applicant compare Chen's device with the instant invention to substantiate applicant's arguments.

It is the examiner's position that the control release device of Chen does not anticipate the instant invention for the sole reason that Chen is lacking in the exemplification of the instant lovastatin. However, Chen clearly suggests the use of lovastatin and the rejection is made under obviousness; thus the prior art need not exemplify lovastatin as argued by the applicant. Chen teaches the pharmokinectics of nifendipine. Therefore, one would have been motivated to substitute nifendipine with the instant lovastatin and expect similar pharmacokinetic values.

With regard to applicant's argument that the instant invention contains a core, a seal coat, an inner coat, an outer coat, and an overcoat, the examiner points out that careful look at Table I

of the instant disclosure does not require a seal coat, an inner coat or a overcoat since the claimed range encompasses zero. Zero clearly implies that the coating is not required. Therefore, applicant's formulation only requires a core and one coating, i.e. an outer coating.

With regard to applicant's arguments that the instant release is different since it contains certain components in certain weight percents, the examiner points out in the instant disclosure, the applicant clearly teaches that the instant invention has the general formula of Table 1. As discussed above, Chen teaches the same device except for the instant lovastatin, thus if applicant's formulation has distinguishing components that provides for the instant functional limitations, then the applicant must claim these patentably distinguishing features.

For the reasons above, the rejection is maintained.

The rejection of claims 76-86 under 35 U.S.C. 103(a) as being unpatentable over Cheng et al, Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical Research (1993), 10:1683-1687 is maintained. The rejection of claim 87 is withdrawn.

Cheng et al teach controlled release device containing lovastatin and a sustained release matrix. Cheng discloses that lovastatin hydrolyzes in vivo to form its corresponding beta-hydroxyacid, which are potent inhibitors of HMG-CoA reductase. See page 1683. Further, Cheng discloses that the liver, the target organ, more efficiently extracts lovastatin and simvastatin than their corresponding beta-hydroxyacid. Thus, the use of controlled release device allows for an equal or better therapeutic value. Table II teaches the total HMG-CoA reductase inhibitors (lovastatin and its acid form) pharmacokinetic parameters (AUC, the Cmax, Tmax,

AUC ratio of 0.94, 1.03, 0.43, and 0.52, and Cmax ratio of 0.66, 0.64, 0.16, and 0.13) in dogs receiving various lovastatin dosage forms. See page 1685. Table V teaches the pharmacokinetics of simovastin administered to humans. See page 1687.

Cheng et al does not specify the pharmacokinetics of lovastatin in humans.

Although Cheng utilizes an animal model, it is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Alberts et al and apply the disclosure to treat humans with the controlled release dosage form to provide for similar pharmacokinetic parameters. One would be motivated to do so since it is conventional in the pharmaceutical industry and its research to draw conclusions from animal models and apply them to humans. Furthermore, Cheng teaches the administration of the dosage forms to humans and dogs, thus one of ordinary skill in the art can ascertain that the controlled release form will also provide similar pharmacokinetics in humans. Thus, absent unexpected results demonstrating that controlled release devices work differently in dogs versus humans, it is the examiner's position that Cheng teaches a similar device, which would yield similar functional limitations.

Response to Arguments

Applicant argues that the instant invention is directed to increasing bioavailability of lovastatin and Cheng et al teach the controlled release device decreases bioavailability. Applicant further argues that SRT8 and SRT14 are irrelevant since Cheng states that SRT8 and SRT14 dosage forms showed little evidence in vivo.

Applicant's arguments filed 2/10/05 have been fully considered but they are not persuasive. Firstly, it is acknowledged that the formulations of CRS8 and CRS14 both decreased bioavailability of lovastatin compared to the immediate release (CT). However, it is the

examiner's position that SRT8 and SRT14 are relevant. Although Cheng teaches that SRT8 and SRT14 were dropped from further testing, nonetheless SRT14 is disclosed as having a higher bioavailability of lovastatin compared to the immediate dosage form. A known composition does not become patentable simply because it has been described as inferior compared to another product for the same use. See in re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). In instant case, applicant is claiming a product and clearly Cheng teaches a sustained release device with lovastatin that has a higher bioavailability than the immediate release as seen in Table II. If applicant has indeed found a controlled device that has the capability of functioning better in vivo, the applicant must claim the patentability-distinguishing feature. The instant invention as presently claimed is not patentably distinguishable over Cheng's SRT8 and SRT14 device since Cheng teaches all the claim limitations: 1) a controlled release device, 2) the instant active lovastatin, 3) and the functional limitation that the device provides a higher bioavailability than an immediate release device.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 76-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,916,595 and 6,485,748. Although the conflicting claims are not identical, they are not patentably distinct from each other because since they encompass similar subject matter.

US '595 is directed to a controlled release oral solid dosage form containing hydroxyl substituted naphthalene compound selected from the group consisting of mevastatin, pravastatin, simvastatin, and lovastatin. The dosage form contains a compressed core containing the medicament and an outer coating layer. US '748 is also directed to a controlled release oral solid dosage form containing a compressed core with a slightly soluble medicament and a membrane coating. The specification defines lovastatin as a drug that is slightly soluble.

Instant application is directed to a controlled release oral solid dosage form for the reduction of serum cholesterol levels containing lovastatin and a controlled release carrier wherein the said dosage form has certain functional limitations upon consumption of the said dosage form.

Although US patent does not claim the functional limitation as seen in instant application, the controlled dosage form of US patent '595 would function in a similar manner as instantly claimed dosage form since both claim the same drug and the same controlled release structure. Although US patent '748 recites a generic slightly water-soluble drug, the specification defines lovastatin as a drug that falls within this category on column 3, line 2. Thus, the instant application and US patents are related genus-species, wherein instant application recites the species and falls within the generic scope of the US patents '748.

Response to Arguments

Applicant argues that US '595 and '748 do not claim or teach a controlled dosage form that increases the bioavailability of lovastatin.

Applicant's arguments filed 2/10/05 have been fully considered but they are not persuasive. The examiner points out that '595 is claiming a controlled release device for an HMG-Co-Reductase inhibitor, specifically lovastatin. Although, the claims do not recite the instant functional limitation of lovastatin, both US '595 and the instant application have the same structure and thus will function the same way. Claiming a functional limitation of a product does not change the product. Both US patent and the instant application are directed to the same product containing the same drug but claimed in a different manner and thus are obvious over each other.

With regard to US '748, '748 also claims the same structure and claims the medicament is a slightly to practically insoluble in water at 25 degrees Celsius. The specification defines lovastatin as a drug that falls into this definition. Thus, the claims of instant application and US '748 have overlapping subject matter. Again claiming a functional limitation of a product does not change the product itself; thus the instant product and US patent are obvious over each other.

Conclusion

All the claims remain rejected at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
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